DOI:
10.1016/j.jelectrocard.2018.01.009

Document Version
Peer reviewed version

Relationship between vectorcardiographic QRS_{area}, myocardial scar quantification, and response to Cardiac Resynchronization Therapy

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Running title:

Vectorcardiography and cardiac magnetic resonance imaging defined scar

Structured abstract

Purpose: To investigate the relationship between vectorcardiography (VCG) and myocardial scar on cardiac magnetic resonance (CMR) imaging, and whether combining these metrics may improve cardiac resynchronization therapy (CRT) response prediction.

Methods: Thirty-three CRT patients were included. QRS_{area}, T_{area} and $QRST_{area}$ were derived from the ECG-synthesized VCG. CMR parameters reflecting focal scar core ($Scar_{2SD}$, $Gray_{2SD}$) and diffuse fibrosis (pre-T1, extracellular volume [ECV]) were assessed. CRT response was defined as ≥15% reduction in left ventricular end-systolic volume after six months' follow-up.

Results: VCG QRS_{area}, T_{area} and $QRST_{area}$ inversely correlated with focal scar (R=-0.44–-0.58 for $Scar_{2SD}$, $p \leq 0.010$), but not with diffuse fibrosis. $Scar_{2SD}$, $Gray_{2SD}$ and QRS_{area} predicted CRT response with AUCs of 0.692 (p=0.063), 0.759 (p=0.012) and 0.737 (p=0.022) respectively. A combined ROC-derived threshold for $Scar_{2SD}$ and QRS_{area} resulted in 92% CRT response rate for patients with large QRS_{area} and small $Scar_{2SD}$ or $Gray_{2SD}$.

Conclusion: Incremental predictive value for CRT response is achieved by a combined CMR-QRS_{area} analysis.

Keywords

Vectorcardiography, myocardial scar, cardiac magnetic resonance imaging, cardiac resynchronization therapy

Highlights

- The relationship between vectorcardiography (VCG) and myocardial scar defined by cardiac magnetic resonance imaging (CMR) is elucidated.
- VCG QRS_{area} significantly inversely correlates with focal scar, suggesting that myocardial scar leads to a smaller QRS_{area}.
- By combining QRS_{area} and CMR focal scar assessment, CRT response prediction improves beyond that by either VCG or scar parameters alone.

Financial disclosures

UCN received a Kootstra Talent Fellowship research grant from Maastricht University and was additionally funded by a research grant from the Dutch Heart Foundation (grant #2015T61). FWP has received research grants from Medtronic, Abbott, LivaNova, Biosense Webster, MSD, and Biotronik. KV received research grants from Medtronic and Abbott. CAR Receives Research Funding and Honoraria from Medtronic, Abbott, LivaNova and Boston Scientific. SC received funding from the Biomedical Research Council and St. Jude Medical. The authors further declare that no competing interests exists.

Conflict of interests

There are none conflict of interests.

Introduction

Cardiac resynchronization therapy (CRT) is an effective treatment for patients with symptomatic heart failure (HF), reduced systolic left ventricular (LV) function, and wide QRS complex. Nevertheless, about one-third of patients eligible according to current guidelines fail to benefit from CRT. Suboptimal CRT response has been attributed to factors including QRS duration (QRSd) <150 ms, non-left bundle branch block (non-LBBB) morphology, ischemic cardiomyopathy, and suboptimal LV lead position.(1)

Parameters derived from the three-dimensional (3D) vectorcardiogram (VCG) have recently been shown to be more accurate than QRSd or morphology in predicting CRT response.(2) The VCG represents the electrical heart vector in three orthogonal directions (X, Y, and Z) and can be derived from a true VCG lead system or synthesized from the standard 12-lead ECG using a mathematical transformation matrix.(3) The 3D area of the VCG QRS- (QRS_{area}) and T-loop (T_{area}) are supposed to reflect unopposed electrical forces during ventricular depolarization and repolarization respectively. Both QRS_{area} and T_{area} have been shown to be strong predictors for LV reverse remodeling after CRT.(2, 4) In a small study it was observed that QRS_{area} was relatively reduced in patients with ischemic cardiomyopathy, suggesting an association between QRS_{area} and myocardial scar.(4)

Ischemic cardiomyopathy, the presence and size of scar burden, and positioning the LV lead in scar are negatively associated with CRT outcome.(5) CMR is able to characterize different types of myocardial scar including focal scar with delayed enhancement (DE-CMR) and diffuse fibrosis with T1 mapping. Recent work demonstrated that focal scar, but not diffuse fibrosis, was associated with poor CRT response.(6)

Summarizing the above literature, it appears that certain electrical characteristics from the VCG and low myocardial scar burden is favorable for response to CRT. The association between VCG and myocardial scar as measured by CMR is however not known.

The purpose of this study was therefore to investigate the association between VCG parameters and myocardial scar (both focal and diffuse) on CMR in HF patients with ventricular conduction disturbance, and whether combining VCG with CMR scar parameters improves prediction to CRT response.

Methods

Study population

Consecutive patients referred for CRT device implantation who underwent CMR imaging as part of their clinical workup were prospectively enrolled at Guys and St Thomas' NHS Trust hospital as previously described.(6) The South-East London Research Ethics Committee approved the study protocol and all patients gave written consent.

Vectorcardiography analyses

Standard 12-lead ECG's were recorded prior to CRT implantation in supine position using the ECG machine MAC 5500 HD (GE Healthcare, Chicago, IL). The digital PDF ECG files with vector graphics were used to extract the original digital ECG-signal. VCGs were semi-automatically synthesized from these digital ECG signals using custom software programmed in MATLAB.(4) The Kors transformation matrix was used to transform the 12-lead ECG to VCG.(3) The onset and end of the QRS-complex and T-wave were manually set on the three overlaid orthogonal leads (X, Y, and Z) of the VCG by two electrophysiologists blinded to CRT outcome. QRS_{area}, T_{area}, and $QRST_{area}$ were defined as the 3D areas of respectively the QRS-, T-wave, and QRST loop from the VCG between the loop and baseline in X, Y, and Z direction calculated as $QRS_{area} = (QRS_{area,x}^2 + QRS_{area,y}^2 + QRS_{area,z}^2)^{1/2}$, $T_{area} = (T_{area,x}^2 + T_{area,y}^2 + T_{area,z}^2)^{1/2}$, and $QRST_{area} = (QRST_{area,x}^2 + QRST_{area,y}^2 + QRST_{area,z}^2)^{1/2}$.(4)

Cardiac magnetic resonance imaging

Patients underwent CMR prior to their CRT implantation using a 1.5T scanner with a 32–channel coil (Philips Healthcare, Best) as described previously.(6) Two independent CMR experts, blinded to CRT outcome, assessed the CMR images. In case of discrepancy, consensus between the reviewers was reached. LV mass was quantified using CMR42 (Circle Cardiovascular Imaging Inc, Calgary) software and used to index the delayed enhancement (DE-CMR) quantification of focal scar. The extent of scar core was automatically quantified using the 2-standard deviation (2SD) method, defined as the region with signal intensity (SI) >2SD above reference myocardium ($Scar_{2SD}$). The extent of Gray zone was quantified by the difference in SI between $Scar_{2SD}$ and $Scar_{3SD}$ ($Gray_{2SD}$).

Conceptually scar core comprises dense and non-viable fibrosis, creating zones of conduction block. Grayzone comprises an admixture of viable and non-viable myocytes, creating zones of slow conduction which may alter to electrical and mechanical remodeling. Both metrics are clinically relevant in the context of LV function and mortality. Given that the burden of scar core, i.e. homogeneously non-viable myocardium, is ubiquitously high amongst advanced heart failure patients, the assessment of the remaining viable tissue may play an important role in predicting the capacity of the LV to positively remodel with CRT. Grayzone is an independent predictor for mortality after myocardial infarction and is associated with ventricular arrhythmias,(7, 8) while focal scar is associated with clinical outcome and LV reverse remodeling after cardiac resynchronization therapy (CRT).(9, 10)

All DE-CMR scar parameters were expressed as a percentage of LV mass (%LV). T1 relaxation maps were processed using a customized software plugin with Osirix (Pixmeo, Geneva), from which the diffuse fibrosis parameters pre-contrast T1 (pre T1) and extracellular volume index (ECV) was calculated.(6) A graphical representation of the VCG and CMR assessment is provided in Figure 1.

Cardiac resynchronization therapy implantation and response determination

The LV lead was preferentially targeted in a posterolateral, lateral or anterolateral coronary sinus tributary, with pacing sites preferentially chosen in a basal position remote from CMR scar. Trans-thoracic echocardiography was assessed pre- and six months post-CRT implantation using a GE Vivid 7 scanner (General Electric-Vingmed, Milwaukee, Wisconsin). Standard 2D images of LV dimensions and ejection fraction (LVEF) were acquired in standard apical 2- and 4-chamber views. LV end-diastolic and end-systolic volumes (LVEDV, LVESV) were used to estimate LVEF using the 2-dimensional modified biplane Simpson's method (EchoPac 6.0.1, General Electric Vingmed). CRT response was defined as an echocardiographic LVESV reduction of ≥15% of baseline afters six months' follow-up. Echocardiography was performed by sonographers blinded to both VCG and CMR data.

Statistical analyses

Statistical analyses were performed using SPSS 24.0 (SPSS Inc., Chicago, Illinois) and MATLAB (Matlab 2016B, MathWorks, Natick, MA). Continuous variables are expressed

as mean±SD or median and interquartile range (IQR) and dichotomous variables in frequencies and percentages. Spearman correlation analyses were carried out between and within VCG and CMR parameters. Parameter differences between CRT responders vs. non-responders were compared using Mann Whitney U-tests. Receiver operating characteristics (ROC) curves were generated to evaluate the diagnostic accuracy of all parameters in identifying CRT response and to find optimal cut-off values. These cut-off values were used to dichotomize the population to groups ≤cut-off and >cut-off, and the number of CRT responders for every subgroup were compared using Chi-squared analyses. The most promising VCG and CMR scar parameters were combined in a cross-tab to evaluate its joint effect on CRT response prediction. Differences within the crosstabs were evaluated using Fisher's exact tests. Significance was defined as *p*-value <0.05 using two-tailed analysis.

Results

Study population

Thirty-three consecutive patients with either non-ischemic (*n* = 17) or ischemic (*n* = 16) cardiomyopathy were included. Patient characteristics are provided in Table 1.

Cardiac resynchronization therapy response

Nineteen out of 33 patients (58%) showed a reduction in LVESV of ≥15% after six months follow-up. Mean $Scar_{2SD}$ and $Gray_{2SD}$ tended to be lower in CRT responders than in non-responders, although this difference was significant for $Gray_{2SD}$ (p<0.011), but it did not reach a significance level for $Scar_{2SD}$ (p=0.065). Pre-T1 and ECV however did not differ between CRT responders and non-responders (p=0.152 and 0.706, respectively). QRS_{area}, but not T_{area} or $QRST_{area}$, was significantly higher in responders than in non-responders to CRT (p = 0.021; Table 2).

There was a positive correlation between $Scar_{2SD}$ and $Gray_{2SD}$ and ΔLVESV (R: 0.46-0.55, p≤0.008), while there was no significant correlation between Pre-T1 and ECV and ΔLVESV. From the VCG parameters, QRS_{area} and $QRST_{area}$ inversely correlated with ΔLVESV (both R: -0.44, p = 0.010), while there was no correlation with ΔLVESV for QRSd and T_{area} (Figure 2).

QRS_{area} and focal scar burden between non-ischemic (*n* = 17) and ischemic patients (*n* = 16) were additionally compared. QRS_{area} was lower (p = 0.046) in patients with

ischemic cardiomyopathy (median: 62, IQR: 27-83) compared to patients with non-ischemic cardiomyopathy (median: 106, IQR: 58-145), while focal scar burden did not differ between the two groups (all p >0.136)

ROC analyses for CMR and VCG parameters identifying CRT response

Pre-T1 and ECV were poor predictors for CRT response, while $Scar_{2SD}$ and $Gray_{2SD}$ were substantially better at predicting CRT response ([AUC: 0.692, p=0.063] and [AUC: 0.759, p=0.012] respectively). QRS_{area}, but not QRSd, T_{area} or $QRST_{area}$, significantly predicted CRT response (AUC: 0.737, p = 0.022) (Figure 3, Table 3).

Association between VCG and myocardial scar

There was no association between pre-T1 or ECV and QRS_{area} or T_{area} (all p>0.142). All VCG parameters inversely correlated with $Scar_{2SD}$ and $Gray_{2SD}$.The strongest VCG-CMR association was found between QRS_{area} and focal scar parameter $Scar_{2SD}$ (Figure 4).

Combining VCG and CMR scar parameters

The study population was dichotomized using the cut-off values for $Scar_{2SD}$, $Gray_{2SD}$ and QRS_{area} derived from the ROC analyses in Table 3. The percentage of CRT responders was significantly higher in patients with low $Gray_{2SD}$ and low $Scar_{2SD}$ versus patients with high focal scar parameters (Figure 5A). The percentage of CRT response was also higher in patients with high QRS_{area} as compared to those with low QRS_{area} (Figure 5B). Crosstab analyses between QRS_{area} and $Gray_{2SD}$/$Scar_{2SD}$ showed that the percentage CRT response was highest (92%) in patients with a combination of high QRS_{area} (>66 mV.ms) and low $Gray_{2SD}$ (≤5.91% LV mass)/low $Scar_{2SD}$ (≤20.29% LV mass). The four subgroups in $Scar_{2SD}$+QRS_{area} combinations differed significantly from each other (overall: p<0.001; Figure 5C). For $Gray_{2SD}$+QRS_{area} combinations, the subgroup [low $Gray_{2SD}$+high QRS_{area}] was significantly different from the other three subgroups, while the subgroups [low $Gray_{2SD}$+low QRS_{area}] and [high $Gray_{2SD}$+high QRS_{area}] were not significantly different.

Discussion

The present study is the first to investigate the relationship between VCG parameters and CMR defined scar, and between these parameters and CRT response. The principal findings of this study are that QRS_{area} significantly correlated inversely with focal scar,

suggesting that myocardial scar leads to a smaller QRS_{area}, Additionally, by combining QRS_{area} and CMR focal scar assessment, CRT response prediction improves beyond that by either VCG or scar parameters alone.

The role of VCG in clinical context

The VCG technique was first described almost a century ago. VCG measures the electrical activity of the heart as a vector loop consisting of momentary magnitudes and directions in 3D space for each time point in the heart cycle. Various VCG systems have been introduced, from which the Frank VCG system (employing seven recording electrodes) was the most common VCG system in clinical care in the 1960s together with the current 12-lead ECG system.(11) After two periods of discontinuation in clinical practice, interest in the use of VCG regained in the late 1980s, and mathematical matrices were developed to synthesize the VCG from the 12-lead ECG.(3) Advantages of VCG parameters over the 12-lead ECG-derived morphology definitions (like LBBB) is that VCG parameters are objective continuous parameters and therefore more suitable for statistical analyses. QRS_{area} and T_{area} defined as the 3D integral of the QRS- and T-wave loop respectively, resemble dispersion of depolarization and repolarization, and are the most common VCG parameters recently investigated in CRT.(2, 4, 12-14)

The association between VCG and CMR scar

The usefulness of VCG for identification of myocardial scar has been investigated by Bizarro et al. almost four decades ago.(15) In this small study, automatically generated VCG parameters from both the QRS- and T- loop were able to identify 85% of the patients with autopsy-confirmed scar. Ever since, the majority of studies have focused on comparing features from the 12-lead ECG with myocardial scar.(16, 17) However, the use of these ECG criteria in estimating scar extent is complex and particularly debatable in patients ventricular conduction disturbances.(17)

In the present study, correlation analyses suggested that QRS_{area} decreased with focal scar burden (encompassing dense scar core), and to a lesser extent scar border zone; but VCG parameters were not significantly associated with measures of diffuse fibrosis. This suggests that scar tissue with higher density affects the VCG 3D loop the most.

A low QRS_{area} theoretically resembles less dispersion and subsequently a small amount of unopposed forces during ventricular depolarization. The size of these forces likely

depends on the uniformity of slow conduction and the amount of viable myocardium. A lower number of viable myocardial cells, lateralization of connexins, and increased axial resistivity after myocardial infarction may lead to a decrease of total electrical forces during the cardiac cycle and therefore an overall decrease of VCG amplitude, and subsequently low QRS_{area} and T_{area}.(18)

QRS_{area} is not only affected by the severity of focal myocardial scar, but may also be affected by the etiology of heart failure alone. Van Deursen et al.(4) reported lower QRS_{area} in patients with ischemic cardiomyopathy compared to patients with non-ischemic cardiomyopathy.

The role of VCG in CRT response prediction

The significant association of a large QRS_{area} with more LV reverse remodeling after CRT is in line with earlier studies demonstrating a significant association of QRS_{area} with CRT response.(2, 4) QRS_{area} has been shown to be associated with delayed electrical activation on the LV lateral wall.(19) QRS_{area} is thought to represent unopposed ventricular contraction forces. A larger QRSarea therefore reflects a greater degree of ventricular electrical dyssynchrony which is amenable to CRT.(4, 20)

The strength of QRS_{area} in predicting CRT response is particularly demonstrated in the recent multicenter prospective MARC study where numerous clinical, echocardiographic, blood, and electrocardiographic biomarkers were studied and related to LV reverse remodeling.(2) From all these biomarkers, only QRS_{area} and echocardiographic interventricular mechanical delay and apical rocking remained significantly associated with LV reverse remodeling in the multivariable model. Although in their data T_{area} showed a significant association with LV reverse remodeling in the unadjusted model (p-value <0.001), significance was not preserved in the multivariate model.(2) Interestingly, T_{area} proved to predict CRT response slightly better than QRS_{area} in retrospective studies by Engels and Vegh et al.(4, 13) The sum of the absolute QRST integral (SAI QRST) has also been investigated as a predictor for LV reverse remodeling. In 234 CRT recipients from the SMART-AV trial by Tereshchenko et al.(14) found that patients with a high $QRST_{area}$ had significantly greater odds of LV reverse remodeling than those with lower $QRST_{area}$. $QRST_{area}$ was also associated with ΔLVESV reduction in our data but was not a significant CRT response predictor in the

ROC analyses (p = 0.074). Altogether these results indicate that the role for T_{area} in CRT response prediction is not fully understood yet.(4, 13, 14)

The relevance of myocardial scar regarding CRT response

The association between focal scar burden and poor CRT response has been investigated in numerous studies. Chalil et al. demonstrated that CRT recipients with a scar size of <33% showed significantly more favorable clinical response to patients with ≥33% scar. Patients with a posterolateral scar, the common site for LV lead placement, also had a higher risk of cardiovascular death and HF hospitalization.(9) Leyva et al. concordantly studied the use of DE-CMR to guide LV lead placement remote from scar tissue in a large cohort of 559 patients. In their data, patients with DE-CMR confirmed scar showed the highest risk of cardiovascular death and lowest echocardiographic CRT response, confirming the importance of pacing remote from scar.(5)

After the introduction of T1 mapping in CMR, a few studies additionally investigated the potential role of diffuse fibrosis in CRT response.(6, 21) The association between diffuse fibrosis and focal scar and LV reverse remodeling was studied by Chen et al. prospectively in CRT candidates with ischemic and non-ischemic etiologies of HF.(6) In a multivariate model only focal scar burden, but not diffuse fibrosis, was able to predict LV reverse remodeling significantly. Höke et al investigated the association of diffuse fibrosis with CRT response prediction specifically in the non-ischemic cohort (21). In their data both focal scar as well as diffuse fibrosis were associated with LV reverse remodeling after CRT. These findings indicate that diffuse fibrosis may have a potential role in CRT response prediction in patients with non-ischemic cardiomyopathy.

Combining VCG with CMR for a better CRT response prediction

The present study demonstrates that combining parameters reflecting both electrical and tissue substrate for CRT may be an approach to further improve CRT response prediction. Almost all (92%) patients with a low extent of focal scar and a large QRS_{area} were CRT responders. This finding is important, since myocardial scar burden and QRS_{area} are inversely related to each other. Apparently, CRT response prediction is better when incorporating focal scar metrics in addition to QRS_{area} compared to using QRS_{area} alone. Potential explanations for the negative effect of scar on CRT may be that 1) scar is inherent to non-viable myocytes and therefore reduces the amount of normal

myocardium that can be resynchronized, 2) pacing in scar may reduce resynchronization as electrical propagation may be inhibited by slow conducting (scarred) myocardium .

Clinical implications

The present study supports the earlier findings that QRS_{area} may improve the selection of CRT candidates and extents this idea by demonstrating that further improvement in selection may be obtained by combining scar characterization using CMR and VCG analysis. The refined positive predictive value using such combined VCG-CMR focal scar index is highly encouraging, in particular in the ischemic cardiomyopathy cohort, in whom the CRT response is commonly low.(22)

Limitations

This study incorporated a relative small number of patients from a single center with the inherent limitation of such study design. Nevertheless, the consecutive patient's cohort reflects a broad real-world experience.

QRS_{area} in the present study is slightly lower compared to previous publications,(5, 6) which may be explained by the lower QRS duration and fewer LBBB morphologies in our study population compared to the populations from Maass et al.(6) and Engels et al.(4) The optimal thresholding values for the scar VCG parameters should be taken in the context of the study and a larger population study is needed to validate these optimal thresholding values and different cut-offs may be required in ischemic and non-ischemic cardiomyopathy.

Conclusion

Focal scar CMR parameters and QRS_{area} are independent predictors for CRT response and are inversely associated with each other. The highest percentage of CRT response was observed in patients with low focal scar CMR values and high QRS_{area}, indicating that combined CMR-VCG parameters may improve prediction to CRT response.

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449 **Table 1**

450 Patient characteristics

Demographics		QRS_{area} *p*-value
Total patient no.	33	
Age (years)	65±12	0.569
Male	27 (82%)	0.479
Ischemic cardiomyopathy	16 (49%)	0.045*
NYHA (II/III/IV)	1 (3%) / 31 (94%) / 1 (3%)	0.270
LVEF (%)	24±8	0.681
ECG QRS duration (ms)	150±22	0.016*
ECG LBBB morphology	12 (36%)	<0.001*
CRT response (reduction ΔLVESV ≥15%)	19 (58%)	0.021*

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452 Values are displayed as mean and standard deviation or n (%). The association between patient
453 characteristics and QRS_{area} was investigated using Spearman correlation analyses for
454 continuous variables and Mann Whitney u or Kruskal Wallis tests for dichotomous variables.

455 BMI=body-mass-index, EDV=end-diastolic volume, ESV=end-systolic volume, LBBB=left bundle
456 branch block, LV=left ventricular, LVEF=LV ejection fraction, NYHA=New York Heart
457 Association.

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Table 2

Parameter value differences between responders and non-responders to CRT

	CRT non-responders (*n*=14)	CRT responders (*n*=19)	*p*-value
T1 mapping (diffuse fibrosis)			
Pre-T1 (ms)	1063 (984-1098)	1065 (1002-1105)	0.706
ECV (%)	0.33 (0.29-0.37)	0.29 (0.24-0.35)	0.152
DE-CMR (focal scar)			
$Gray_{2SD}$ (%)	7.27 (5.48-10.37)	3.83 (1.69-6.10)	0.011*
$Scar_{2SD}$ (%)	26.16 (18.69-28.84)	13.29 (4.55-26.83)	0.065
VCG parameters			
QRSd (ms)	145 (125-161)	151 (144-168)	0.199
QRS_{area} (mV.ms)	59 (33-78)	106 (62-163)	0.021*
T_{area} (mV.ms)	41 (32-63)	42 (25-90)	0.577
$QRST_{area}$ (mV.ms)	33 (29-68)	57 (34-85)	0.077

Responders are defined as reduction of LVESV ≥15%. P-values are based Mann Whitney u-tests. Continuous variables are displayed as median and interquartile ranges. *indicates significance (*p*-value ≤0.05).

Table 3

ROC analyses predicting CRT response (ΔLVESV ≥15%) for CMR and VCG parameters

	AUC	CI	*p*-value	Threshold	Sensitivity	Specificity
T1 mapping (diffuse fibrosis)						
Pre-T1 (ms)	0.461	0.258-0.663	0.702	<1063	47%	50%
ECV (%)	0.650	0.455-0.846	0.145	<0.32	68%	72%
DE-CMR (focal scar)						
$Gray_{2SD}$ (%)	0.759	0.586-0.933	0.012*	<5.91	74%	71%
$Scar_{2SD}$ (%)	0.692	0.503-0.881	0.063	<20.29	68%	72%
VCG						
QRSd (ms)	0.635	0.438-0.832	0.190	>148	63%	57%
QRS_{area} (mV.ms)	0.737	0.564-0.910	0.022*	>66	74%	71%
T_{area} (mV.ms)	0.560	0.358-0.762	0.560	>39	63%	50%
$QRST_{area}$ (mV.ms)	0.684	0.493-0.875	0.074	>36	74%	64%

*indicates significance (*p*-value ≤0.05).

Figure 1

Graphical representation of CMR and VCG assessment approach.

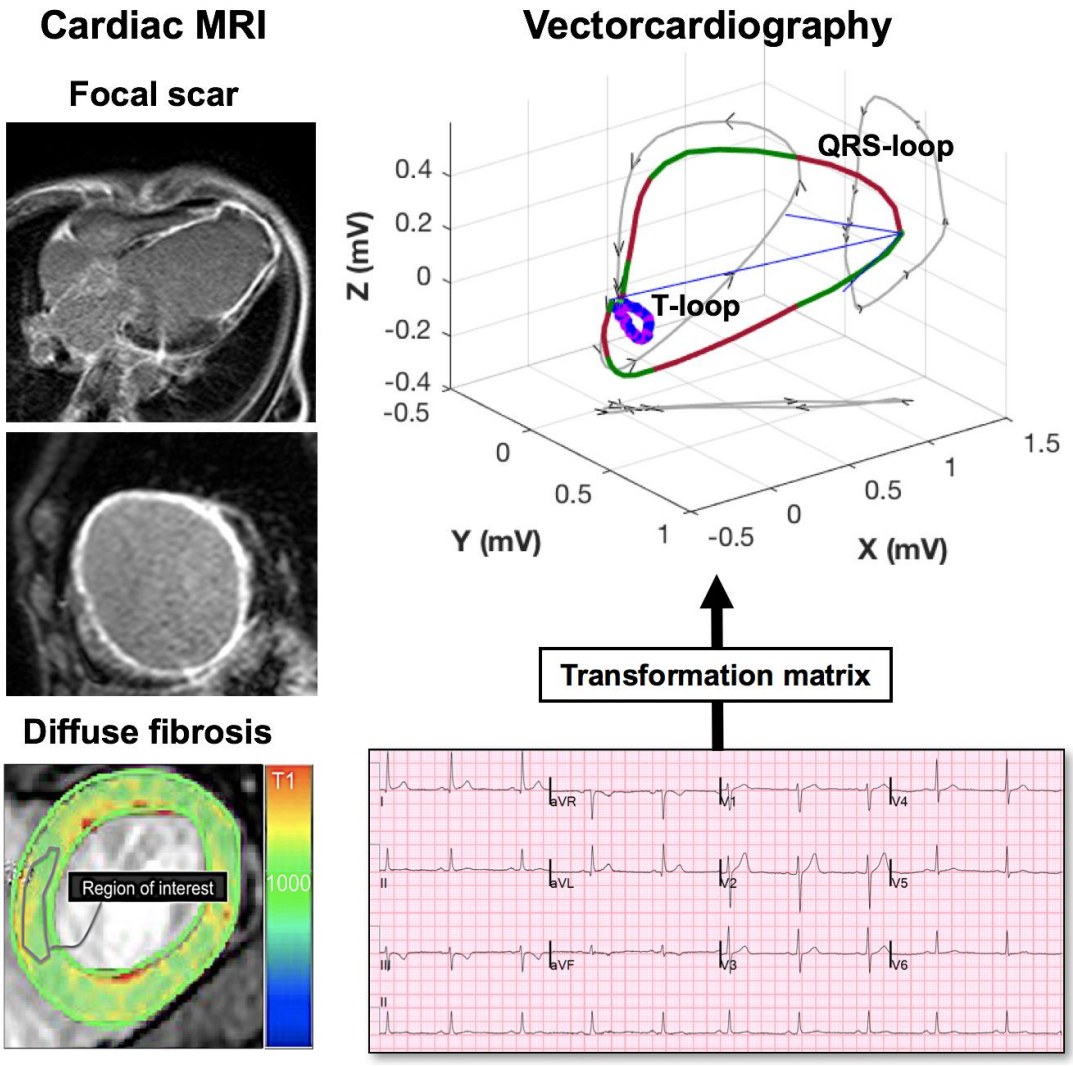

Figure 2

Scatter plots of VCG and CMR scar parameters vs. ΔLVESV (%). Correlation coefficients are based on Spearman correlation analyses.

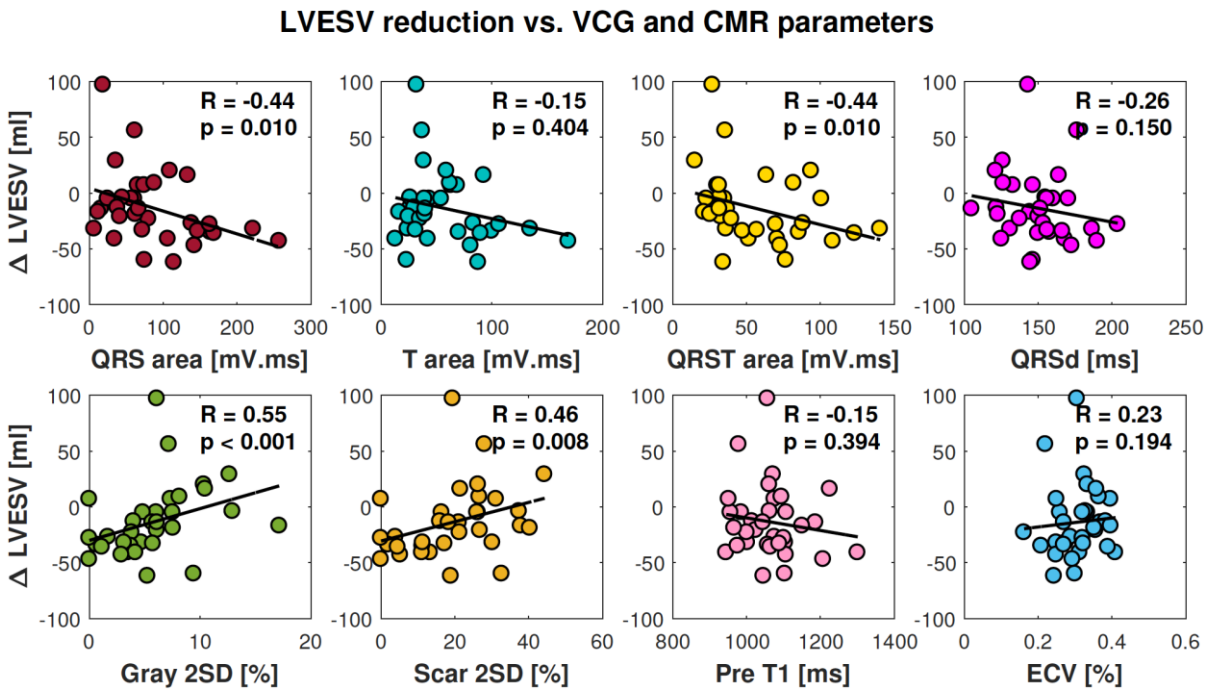

Figure 3

ROC analyses predicting CRT response (ΔLVESV ≥15%) for CMR focal scar parameters (upper left) and VCG parameters (upper right). Accompanying details of the ROC analyses are provided in Table 3.

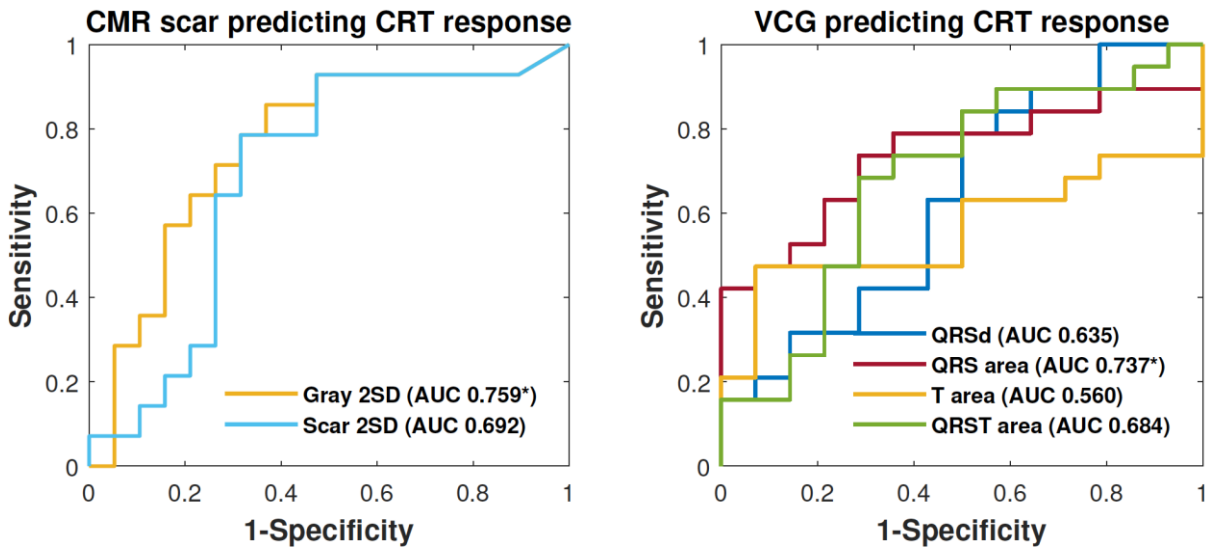

Figure 4

Scatter plots of CMR scar parameters vs. VCG parameters. Correlation coefficients are based on Spearman correlation analyses. All focal scar CMR parameters correlated inversely with the VCG parameter.

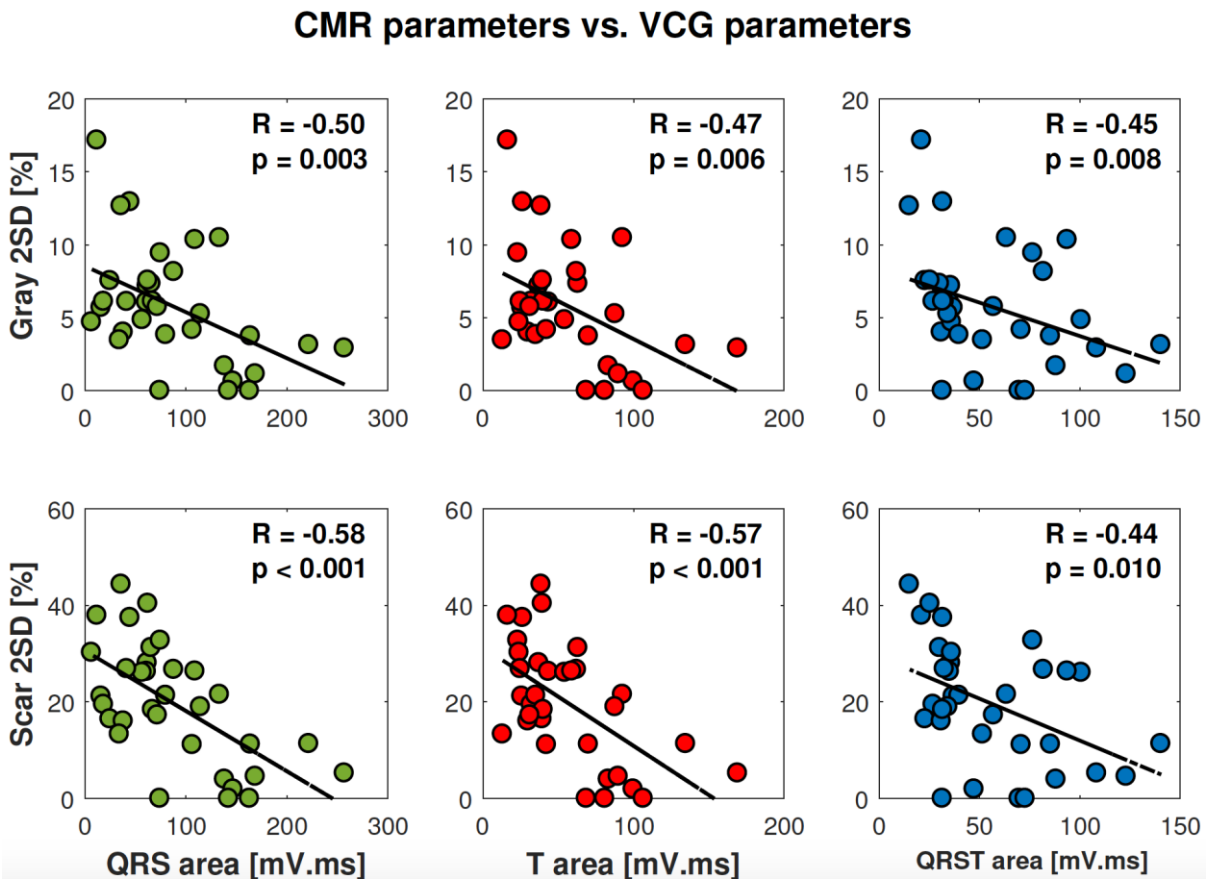

Figure 5

2D bar graphs showing CRT response percentage per focal scar CMR (A) and VCG (B) parameter when dividing the study population using the cut-off value as determined by ROC analyses in Table 3. *P*-values in A and B are based on Chi-squared tests.

3D bar graphs demonstrating CRT response percentage when combining QRS_{area} with focal scar CMR parameters (C). *P*-values in each graph are based on Fisher's exact tests.